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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,738	02/18/2004	Andreas H. Sarris	480208.401C3	1671

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/782,738	SARRIS ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 71-86 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 71-86 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 2-18-04 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9-7-04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims included in the prosecution are 71-86.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 71-79 and 81-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webb (5,741,516) of record by itself or in combination with Mehlhorn (5,762,957) or vice versa (Mehlhorn in view of Webb).

Webb discloses a method of preparation of liposomes containing vinca alkaloids such as vinblastine and vincristine (sulfate). The method involves, a) preparing vinca alkaloid solution b) preparing liposomes containing sphingomyelin and cholesterol with an acidic interior (citrate buffer); 2) adding vincristin sulfate to the external medium; 3) adding disodium hydrogen phosphate to the external medium to create a pH gradient with an external pH of 7.2 to 7.6. The transmembrane gradient created loads vincristine sulfate into the liposomes (abstract, col. 6, line 8 through col. 7, line 12, Examples, Examples 1-2 in particular and claims). What is lacking in Webb is the teaching of the supply of the vinca alkaloid solution (step a in the method), liposomes (step b) and disodium phosphate solution in the form of a kit. However, supply of the reagents to prepare vincristine sulfate loaded

liposomes just before use by the method taught by Webb would have been obvious to one of ordinary skill in the art with a reasonable expectation of success,

Mehlhorn teaches a method of loading liposomes with drugs and a kit for such a method. The method involves preparing the liposomes with acidic interior (citrate buffer), adding a solution to make the exterior of the liposomes basic to create a transmembrane gradient and loading the chemical species (drug). According to Mehlhorn, the reagents, chemical species solution, liposomes and the basic solution are to be supplied in the form of a kit. By such a method according to Mehlhorn, the encapsulation can be done quickly and easily. The fear of degradation of the vesicles and leakage of the chemicals prior to administration need not be a concern, since the chemicals are easily encapsulated in the vesicles usually just before use, and the vesicles containing the chemical can be immediately delivered without further purification or other treatment (abstract, col. 2, line 9 through col. 4, line 61, col. 6, line 12 through col. 10 line 6, Examples and claims). What is lacking in Mehlhorn is the teaching of vinca alkaloids as the chemical species.

It would have been obvious to one of ordinary skill in the art to supply the reagents of Webb in the form of a kit since Mehlhorn teaches that kits can be used for the loading of liposomes with the chemicals by the same method just before use and advantages of such kits. Alternately, the use of vinca alkaloids as the chemical species in the kit of Mehlhorn would have been obvious to one of ordinary skill in the art, with a reasonable expectation of success since Webb teaches the loading method, which is the same as Mehlhorn.

3. Claims 80 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Webb (5,741,516) by itself or in combination with Mehlhorn (5,762,957) or vice versa (Mehlhorn in view of Webb), further in view of Lenk (5,262,168).

The teachings of Webb, and Mehlhorn have been discussed above. What is lacking in these references is the teaching of the use of a cryoprotectant such as mannitol.

Lenk while disclosing prostaglandin liposomal compositions teaches that the liposomes can be loaded using a pH gradient and that the liposomes can be lyophilized using cryoprotectant such as mannitol. An aqueous solution containing the drying protectant is added to encapsulate the drying protectant (abstract, col. 4, lines 15-20, col. 9, line 53 through col. 10, line 6).

To include a drying protectant such as mannitol in the aqueous solution of the kit taught by Mehlhorn, if the goal is to lyophilize the liposomes, would have been obvious to one of ordinary skill in the art with a reasonable expectation of success since Lenk teaches such a use in liposome formulations.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK